

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (currently amended) A method of ~~detecting a polymorphic site in a sample to determine~~ determining alpha-2B-adrenergic receptor function; by detecting a polymorphism at a polymorphic site in a polynucleotide encoding an alpha-2B-adrenergic receptor molecule, the method comprising:
  - a. obtaining ~~the~~ a sample ~~having a~~ of a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide; and
  - b. detecting in the sample a polymorphism at a polymorphic site comprising at least one of nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 ~~or fragment~~ or a complement thereof.
2. (currently amended) A method according to claim 1, wherein the ~~polymorphic site~~ polymorphism comprises SEQ ID NO: 3 or 4 or a complement thereof.
3. (currently amended) A method according to claim 2, wherein the ~~polymorphic site~~ polymorphism is an insertion of 9 nucleotides at nucleotide position 901 to 909 of SEQ ID NO: 1.
4. (currently amended) A method according to claim 2, wherein the ~~polymorphic site~~ polymorphism is a deletion of 9 nucleotides at nucleotide position 901 to 909 of SEQ ID NO: 2.
5. (currently amended) A method according to claim 2, wherein the complement of the ~~polymorphic site~~ polymorphism comprises SEQ ID NO: 5 or 6.

6. (currently amended) A method of genotyping an alpha-2B-adrenergic receptor gene comprising:
  - a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide; and
  - b. detecting in the sample a polymorphism at a polymorphic site comprising at least one of nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 ~~or fragment~~ or a complement thereof.
7. (currently amended) A method according to claim 6, wherein the genotyping is performed on two copies of the alpha-2B-adrenergic receptor gene.
8. (currently amended) A method according to claim 6, wherein the ~~polymorphic site~~ polymorphism comprises SEQ ID NO: 3 or 4 or a complement thereof.
9. (currently amended) A method according to claim 6, wherein the ~~polymorphic site~~ polymorphism is an insertion of 9 nucleotides at nucleotide positions 901 to 909 of SEQ ID NO: 1.
10. (currently amended) A method according to claim 6, wherein the ~~polymorphic site~~ polymorphism is a deletion of 9 nucleotides at nucleotide position 901 to 909 of SEQ ID NO: 2.
11. (currently amended) A method according to claim 6, wherein the complement of the ~~polymorphic site~~ polymorphism comprises SEQ ID NO: 5 or 6.
12. (currently amended) A method according to claim 6, wherein the detection of the ~~polymorphic site~~ polymorphism is by dideoxy sequencing, restriction digestion, allele-specific polymerase reaction, single-stranded conformational polymorphism analysis, genetic bit analysis, temperature gradient gel electrophoresis, ligase chain

reaction, ligase/polymerase genetic bit analysis, or random amplification of DNA.

13. (currently amended) A method of genotyping a polynucleotide encoding an alpha-2B-adrenergic receptor molecule from a sample, comprising: (a) obtaining a sample comprising the polynucleotide; and (b) performing a primer extension reaction employing an oligonucleotide comprising at least one nucleotide comprising a nucleotide sequence homologous to a nucleotide sequence located at position 901 to 909 of SEQ ID NO: 1 or 2 or ~~fragment~~ or a complement thereof.
14. (currently amended) A method according to claim 13, wherein the oligonucleotide comprises a nucleotide sequence having a length of from about 10 to about 50 nucleotides.
15. (original) A method according to claim 13, wherein the primer extension reaction is a single nucleotide primer extension reaction.
16. (currently amended) A method of genotyping an individual by genotyping a polynucleotide encoding an alpha-2B-adrenergic receptor molecule from a sample of an the individual, comprising:
  - a. isolating from the individual a the sample having a polynucleotide encoding an the alpha-2B adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide thereof;
  - b. subjecting incubating the polynucleotide to an incubation with at least one oligonucleotide, the at least one oligonucleotide having a nucleotide sequence that is complementary to a region of the polynucleotide, and which, when hybridized to the region permits the identification of the nucleotide present at a polymorphic site of the polynucleotide, wherein the incubation is under conditions sufficient to allow specific hybridization to occur between complementary nucleic acid molecules;
  - c. permitting ~~the~~ hybridization to occur; and

- d. identifying the polymorphic site to obtain the genotype of the individual, wherein the polymorphic site comprises a polymorphism comprising an insertion or deletion of 9 nucleotides at nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2.
17. (currently amended) ~~A~~ The method according to claim 16, further comprising amplifying the ~~polymorphic site~~ polymorphism of the polynucleotide prior to the hybridization.
18. (currently amended) ~~A~~ The method according to claim 16, wherein the at least one oligonucleotide is selected from the group consisting of
- 5'-GCTCATCATCCCTTTCTCGCT-3' (SEQ ID NO: 13);
- 5'- AAAGCCCCACCATGGTCGGGT-3' (SEQ ID NO: 14);
- 5'-CTGATCGCCAAACGAGCAAC-3' (SEQ ID NO: 15);
- 5'-AAAAACGCCAATGACCACAG-3' (SEQ ID NO: 16);
- 5'-TGTAACGACGGCCAGT-3' (SEQ ID NO: 17);
- 5'-CAGGAAACAGCTATGACC-3' (SEQ ID NO: 18);
- 5'-AGAAGGAGGGTGTGTTGTGGGG-3' (SEQ ID NO: 19);
- 5'- ACCTATAGCACCCACGCCCCT-3'(SEQ ID NO: 20);
- 5'-GGCCGACGCTCTTGTCTAGCC-3' (SEQ ID NO: 21);
- 5'-CAAGGGGTTCTTAAGATGAG-3' (SEQ ID NO: 22); and complementary sequences thereof.
19. (currently amended) ~~A~~ The method according to claim 16, wherein the specific

hybridization is selected from the group consisting of southern blot, dot blot, reverse dot blot, northern blot, and allele-specific oligonucleotide hybridization.

20. (currently amended) A The method according to claim 16, wherein the at least one oligonucleotide is labeled with a label selected from the group consisting of radiolabel, fluorescent label, bioluminescent label, chemiluminescent label, nucleic acid label, hapten label, and enzyme label.
21. (currently amended) A The method according to claim 16, wherein the identity of the polymorphic site is determined by dideoxy sequencing, restriction digestion, allele-specific polymerase reaction, single-stranded conformational polymorphism analysis, genetic bit analysis, temperature gradient gel electrophoresis, ligase chain reaction, or ligase/polymerase genetic bit analysis, or random amplification of DNA.
22. (currently amended) A The method according to claim 16, wherein the at least one oligonucleotide ~~comprises a nucleotide sequence~~ is from about 10 to about 50 nucleotides in length.
23. (withdrawn) A method of detecting a polymorphic site in a sample to determine alpha-2B-adrenergic receptor function, comprising:
  - a. obtaining the sample having an alpha-2B-adrenergic receptor molecule comprising amino acid SEQ ID NO: 7 or 8 or fragment thereof and
  - b. detecting in the sample the polymorphic site at amino acid positions 294 to 309 of SEQ ID NO: 7 or 8.
24. (withdrawn) A method according to claim 23, wherein the polymorphic site comprises SEQ ID NO: 9 or 10.
25. (withdrawn) A method according to claim 23, wherein the polymorphic site is an insertion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 7.

26. (withdrawn) A method according to claim 27, wherein the polymorphic site is a deletion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 8.
27. (withdrawn) A method of detecting a polymorphic site to determine alpha-2B-adrenergic receptor function, comprising:
- a. obtaining a sample having an alpha-2B-adrenergic receptor molecule comprising amino acid SEQ ID NO: 7 or 8 or fragment thereof;
  - b. contacting the sample with an antibody specifically reactive with the polymorphic site at amino acid positions 294 to 309 of SEQ ID NO: 7 or 8; and
  - c. detecting in the sample a complex formed between the antibody and amino acid positions 294 to 309 of SEQ ID NO: 7 or 8.
28. (withdrawn) A method according to claim 27, wherein the polymorphic site is an insertion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 7.
29. (withdrawn) A method according to claim 27, wherein the polymorphic site is a deletion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 8.
30. (currently amended) A method of haplotyping an alpha-2B-adrenergic receptor gene, wherein the gene exists as a first copy and a second copy, the method comprising:
- a. obtaining a sample having apolynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide;
  - b. detecting in the sample a polymorphism at a polymorphic site comprising nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or a fragment or a complement thereof on ~~one~~ a first copy of the alpha-2B-adrenergic receptor gene; and

- c. determining the identity of an additional polymorphic site on the first copy of the alpha-2B-adrenergic receptor gene.
31. (currently amended) A method for ~~determining~~ identifying an individual at increased risk for developing a disease associated with an alpha-2B-adrenergic receptor molecule comprising:
- a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide from the individual; and
  - b. detecting in the sample a polymorphism at a polymorphic site comprising at least one of nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 ~~or fragment or a~~ complement thereof, ~~which wherein the~~ polymorphism correlates to the disease, thereby identifying the individual at increased risk for the disease.
32. (currently amended) ~~A~~ The method of claim 31, wherein the disease is selected from the group consisting of cardiovascular disease, central nervous system disease, and combinations thereof.
33. (currently amended) ~~A~~ The method according to claim 31, wherein the ~~polymorphic site~~ polymorphism comprises SEQ ID NO: 3 or 4 or a complement thereof.
34. (currently amended) ~~A~~ The method according to claim 31, wherein the ~~polymorphic site~~ polymorphism is an insertion of 9 nucleotides at nucleotide position 901 to 909 of SEQ ID NO: 1.
35. (currently amended) ~~A~~ The method according to claim 31, wherein the ~~polymorphic site~~ polymorphism is a deletion of 9 nucleotides at nucleotide position 901 to 909 of SEQ ID NO: 2.
36. (currently amended) ~~A~~ The method according to claim 33, wherein the complement

of the ~~polymorphic site~~ polymorphism comprises SEQ ID NO: 5 or 6.

37. (currently amended) ~~A~~ The method according to claim 31, wherein the alpha-2B-adrenergic receptor molecule comprises SEQ ID NO: 7 or 8 or a fragment thereof.
38. (currently amended) A method for diagnosing or prognosing an individual with a disease associated with an alpha-2B-adrenergic receptor molecule, comprising:
- a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide from the individual; and
  - b. detecting in the sample a polymorphism at a polymorphic site comprising at least one of nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 ~~or fragment or a~~ complement thereof which correlates to the disease, ~~thereby diagnosing or prognosing the disease.~~
39. (currently amended) ~~A~~ The method according to claim 38, wherein the disease is a cardiovascular disease, a central nervous system disease, or combinations thereof.
40. (currently amended) ~~A~~ The method according to claim 38, wherein the ~~polymorphic site~~ polymorphism comprises SEQ ID NO: 3 or 4 or a complement thereof.
41. (currently amended) ~~A~~ The method according to claim 38, wherein the ~~polymorphic site~~ polymorphism is an insertion of 9 nucleotides at nucleotide position 901 to 909 of SEQ ID NO: 1.
42. (currently amended) ~~A~~ The method according to claim 38, wherein the ~~polymorphic site~~ polymorphism is a deletion of 9 nucleotides at nucleotide position 901 to 909 of SEQ ID NO: 2.
43. (currently amended) ~~A~~ The method according to claim 40, wherein the complement of the ~~polymorphic site~~ polymorphism comprises SEQ ID NO: 5 or 6.



44. (currently amended) ~~A~~ The method according to claim 38, wherein the alpha-2B adrenergic receptor molecule comprises SEQ ID NO: 7 or 8 or a fragment thereof.
45. (withdrawn) A method of predicting an individual's response to an agonist or antagonist, comprising:
- a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement of the polynucleotide from the individual;
  - b. detecting in the sample a polymorphic site comprising nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or fragment or complement thereof; and
  - c. correlating the polymorphic site to a predetermined response thereby predicting the individual's response to the agonist or antagonist.
46. (withdrawn) A method according to claim 45, wherein the alpha-2B adrenergic receptor molecule comprises SEQ ID NOS. 7 or 8 or fragment thereof.
47. (withdrawn) A method according to claim 45, wherein the agonist is an alpha-2B adrenergic receptor agonist.
48. (withdrawn) A method according to claim 45, wherein the antagonist is an alpha-2B adrenergic receptor antagonist.
49. (withdrawn) A method according to claim 47, wherein the alpha-2B adrenergic receptor agonist is an agonist selected from the group consisting of epinephrine, norepinephrine, clonidine, oxymetazoline, guanabenz, UK14304, BHT933 and combinations thereof.
50. (withdrawn) A method according to claim 48, wherein the alpha-2B adrenergic receptor antagonist is an antagonist selected from the group consisting of yohimbine,

prazosin, ARC 239, rauwolscine, idazoxan, tolazoline, phentolamine and combinations thereof.

51. (withdrawn) A method according to claim 45, wherein the predetermined response to the agonist or antagonist is correlated to adenyly cyclase, MAP kinase activity, phosphorylation or inositol phosphate levels.
52. (withdrawn) A method according to claim 45, wherein the individual is homozygous for SEQ ID NO: 2 and exhibits a decreased response to the alpha-2B adrenergic receptor agonist.
53. (withdrawn) A method according to claim 45, wherein the individual's response is desensitization to the agonist or antagonist.
54. (withdrawn) A method according to claim 47, wherein the individual's response is desensitization to the alpha-2B-adrenergic receptor agonist.
55. (withdrawn) A method for selecting an appropriate pharmaceutical composition to administer to an individual having a disease associated with an alpha-2B adrenergic receptor molecule, comprising:
  - a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement of the polynucleotide from the individual;
  - b. detecting in the sample a polymorphic site comprising nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or fragment or complement thereof; and
  - c. selecting the appropriate pharmaceutical composition based on the polymorphic site present.
56. (withdrawn) A method of claim 55, wherein the disease is a cardiovascular disease, a central nervous system disease or combinations thereof.

57. (withdrawn) A method according to claim 55, wherein the alpha-2B-adrenergic receptor molecule comprises SEQ ID NO. 7 or 8 or fragment thereof.
58. (withdrawn) A method according to claim 55, wherein the pharmaceutical composition is an alpha-2B-adrenergic receptor agonist or antagonist.
59. (withdrawn) A method according to claim 58, wherein the alpha-2B-adrenergic receptor agonist is an agonist selected from the group consisting of epinephrine, norepinephrine, clonidine, oxymetazoline, guanabenz, UK14304, BHT933, and combinations thereof.
60. (withdrawn) A method according to claim 58, wherein the alpha-2B adrenergic receptor antagonist is an antagonist selected from the group consisting of yohimbine, prazosin, ARC 239, rauwolscine, idazoxan, tolazoline, phentolamine and combinations thereof.
61. (withdrawn) A method according to claim 58, wherein the appropriate pharmaceutical composition to administer is correlated to adenylyl cyclase, MAP kinase, phosphorylation or inositol phosphate activity.
62. (withdrawn) A method according to claim 55, wherein the individual is homozygous for SEQ ID NO: 2 and exhibits a decreased response to the alpha-2B adrenergic receptor agonist.
63. (currently amended) A method of ~~detecting a polymorphic site in a sample to determine~~ determining alpha-2B-adrenergic receptor function; by indirectly detecting a polymorphism at a polymorphic site in a polynucleotide encoding an alpha-2B-adrenergic receptor molecule, the method comprising:
- a. obtaining ~~the a~~ a sample ~~having~~ comprising a polynucleotide encoding an alpha-2B-adrenergic receptor molecule, wherein the polynucleotide, or a fragment or a complement thereof, comprises ~~comprising~~ SEQ ID NO: 1 or 2 ~~or fragment or~~

~~complement of the polynucleotide; and~~

b. indirectly detecting in the sample the polymorphism at the polymorphic site comprising at least one of nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 ~~or fragment~~ or a complement thereof.

64. (withdrawn) A method of detecting a polymorphic site in a sample to determine alpha-2B-adrenergic receptor function, comprising:

a. obtaining the sample having an alpha-2B-adrenergic receptor molecule comprising amino acid SEQ ID NO: 7 or 8 or fragment thereof; and

b. indirectly detecting in the sample the polymorphic site at amino acid positions 294 to 309 of SEQ ID NO: 7 or 8.